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Formulation and Evaluation of Albumin Microspheres of Paracetamol

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ABSTRACT

Medication molecules are sent to the body regions where they are most effective using dosage forms. You ought to attempt inhalation therapy if you want to maximise the benefits of your medicine. Example Inhalants and drugs that dissolve in water or other liquids are examples of fluid dose forms. Explanation-Solution. Ensure that the patient's orifices are not obstructed in order to provide medication. One sort of disintegrator that functions is albumin, which expands when in contact with stomach acid and facilitates the tablet's dissolution. Historically, a variety of oral extended-release dose forms were referred to as "modified release dosage products." The objective of the current study is to create a paracetamol pill that contains microspheres to cover up the bitter taste of the medication and make it easier for children, the elderly.

Keywords- Microsphere, Tablets, Emulsion, Paracetamol.

I. INTRODUCTION

While the contents of a micromatrix are scattered throughout the matrix of the microsphere, those of a microcapsule are contained within the capsule wall. In contrast to micromatrices, where the substance is uniformly dispersed among the microspheres, the substance in microcapsules is enclosed within a clearly defined capsule wall. [1,2,3,4,5,6,7] The drug may have been contained in the particle matrix of biodegradable microspheres, allowing for controlled drug release. A micron to a millimetre in diameter, microspheres are spherical objects. The active component in painkillers is acetaminophen, also referred to as paracetamol or N-acetyl-p-aminophenol. [9,10,11] Paracetamol does not appear to promote tumour growth when compared to phenacetin. This painkiller and fever reducer is available without a prescription and over-the-counter [11,15,16,17,18,19]. Due to the fact that it does not cause the same stomach bleeding that aspirin does, paracetamol is secure and well-tolerated. Salicin and salicylic acid were discovered by chemists in the second half of the nineteenth century. The German chemist Felix Hoffmann of Bayer and the French chemist Charles Frederic Gerhardt (Strasburg, 1816–1856) invented the chemical procedures used to produce acetylsalicylic acid (Ludwigsburg, 1868–Switzerland, 1946). Researchers investigated alternative production methods as the supply of cinchona trees began to decline in the 1880s. Acetanilide and phenacetin, respectively, were discovered in 1886 and 1888. In 1878, Harmon Northrop Morse (1848–1920) reduced p-nitrophenol in glacial acetic acid using tin to produce paracetamol. This medication wasn't commonly taken recreationally prior to Morse's passing. Although paracetamol was initially mistakenly thought to be a byproduct of the drug rather than a metabolite when it was first discovered in the urine of phenacetin users in 1899. Bernard Brodie (1907-1989), a Liverpool native, and Julius Axelrod, a New Yorker, both studied methemoglobinemia, a potentially

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fatal condition in which the blood's capacity to carry oxygen is severely reduced (1912-2004). In 1948, Brodie and Axelrod made the initial connection between methemoglobinemia and acetanilide. Acetanilide's analgesic effect was linked to paracetamol, its active metabolite, and paracetamol was discovered to have no negative effects on acetanilide [15,16,17,18,19].

Tylenol Children's Elixir was released to the market by McNeil Laboratories in 1955 with the intention of lowering fever and pain in young patients. Paracetamol (Panadol) 500 mg tablets were first made available in the UK in 1956. At first, they could only be obtained with a prescription from a doctor and were promoted as a way to lower fever and pain. Contrary to other analgesics like aspirin, paracetamol did not give any study participants stomach upset. Since paracetamol was included in the British Pharmacopoeia in 1963, its reputation as a pain reliever with few side effects and few drug interactions has only grown. [20,21,22,23,24]

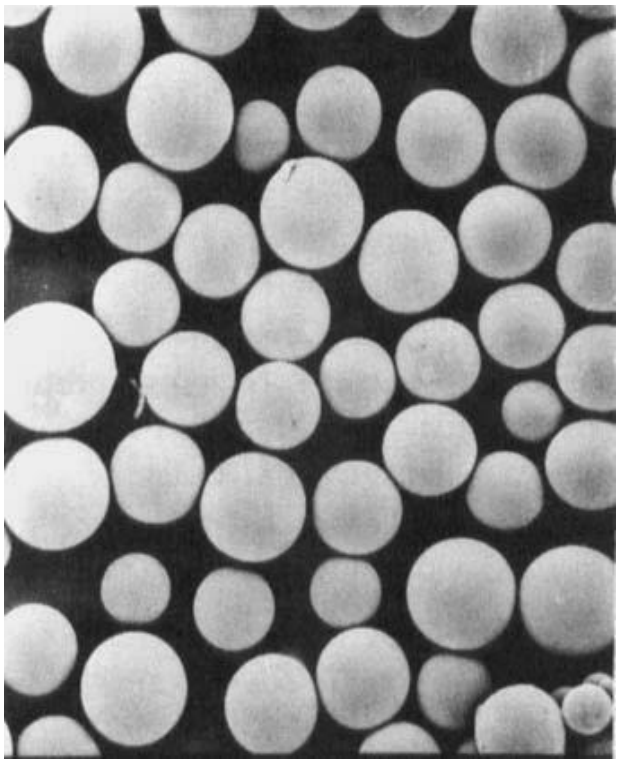

Figure 1: Albumin

II. MATERIAL AND METHODS

All of the reagents and chemicals used in the analysis were purchased from various suppliers; the paracetamol was a free sample provided by Sun Pharma, pvt, ltd in Dehradun; egg albumin, gluteraldehyde, and liquid parafin were purchased from various businesses; and so on.

Microsphere of Egg Albumin preparation

Egg albumin was used to create PCM microspheres using a modified thermal cross-linking technique that did not require an emulsion. [25–29] Light paraffin oil needs to be heated to between 60 and 70 °C while being stirred in order to dissolve 100 cc of it. The food's temperature was lowered to that of room temperature. Give 10 ml of an egg albumin aqueous solution containing a medication to polymer ratio of 1.0:1.0, 1.0:1.5, or 1.0:2.0 drop by drop using a 22-gauge hypodermic syringe. The concentrations of the medication and polymer are 5, 7, 10, and 15%, respectively. A magnetic stirrer was used to agitate the liquid at 600 rpm for 10 minutes, dissolving the light paraffin (Remi equipment, 5 l capacity, Mumbai, India). It resulted in the formation of an emulsifiable mixture. The oil bath was maintained at 95°C until the microspheres were completely dehydrated and no longer sticky, based on preliminary research at four different temperatures (-30°C, -60°C, -80°C, and at 95°C). At this temperature, the greatest number of consistently small, spherical microspheres were created. After being taken out of the oil, the microspheres were rinsed six times for two minutes at 700 rpm in 20 cc of petroleum ether. The microspheres were then air-dried for 24 hours at room temperature (at 25°C 0.5°C, 60% RH) after being rinsed three times with 60 cc of distilled water for two minutes at 700 rpm. To maintain the dry goods' regular temperature, desiccators were utilised. The powder flows readily and is light and golden. To create the microspheres for each batch, different ratios of the medication to egg albumin and the surfactant (span 60; 0.2% wt/vol, 0.4% wt/vol, and 0.6% w/v) were used (1.0:1.0, 1.0:1.5 and 1.0:2.0). Throughout the course of these studies, all other variables were maintained constant. We established the typical size of the microspheres using a micrometre that was calibrated on a stage.

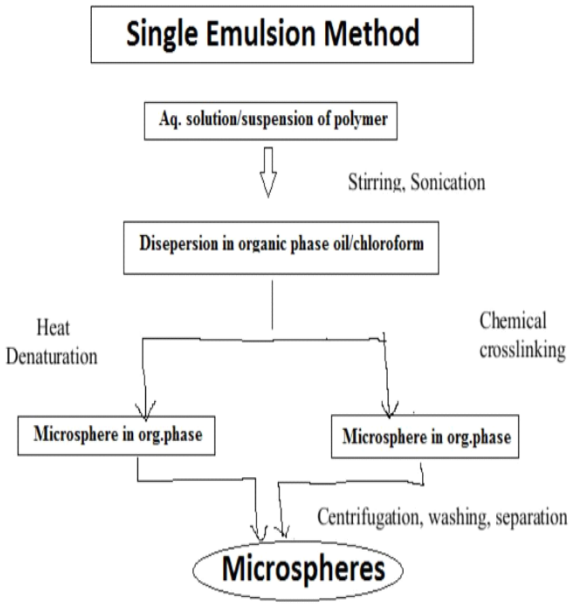

Figure 2: Flow Chart of Microsphere preparation with Emulsion method

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Table 1: Composition of Paracetamol loaded egg albumin Microsphere

Ingredients	Batch code					
	F1	F2	F3	F4	F5	F6
Paracetamol	60	60	60	60	60	60
Egg Albumin conc, % w/v)	10	10	10	20	20	20
Span 60(% w/v)	1	1	1	1	1	1
Vol. of Gluteraldehyde (ml)	0.5	1	2	0.5	1	2

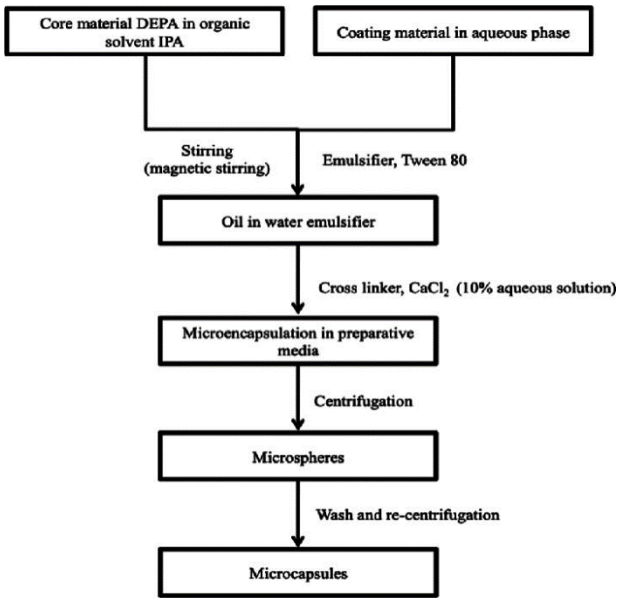

Figure 3: Flow chart of preparation of Microspheres

Evaluation of tablets

A) General Appearance

Five tablets from different batches were randomly selected and organoleptic properties such as color, odor, taste, shape were evaluated. Appearance was judged visually.

B) Thickness and Diameter

Thickness and width of not really settled utilizing Vernier Caliper. Five tablets from each batch were used and an average value was calculated.

C) Drug content

Twenty tablets were taken and measure of medication present in every not really settled. The tablets were squashed in a mortar and the powder identical to 100 mg of medication was moved to 100 ml standard jar. The powder was disintegrated in 50 ml of 0.1 N HCl and made up to volume with of 0.1 N HCl. The example was blended completely and separated through 0.45 µ layer channel. The separated arrangement was weakened appropriately for drug content by UV spectrophotometer at ƛ max of 276 nm using of 0.1 N HCl as blank.

D) Hardness

For each formulation, the hardness of five tablets was determined using the Monsanto hardness tester.

E) Uniformity of weight

Twenty tablets were randomly selected from each batch individually weighted the average weight and standard deviation of 20 tablets was calculated.

F) Friability

The condition of being friable, describes the tendency of a solid substance to break into smaller pieces under duress or contact especially by rubbing or by using Roche Friabilator.

III. DISSOLUTION DATA AND RELEASE RATE KINETICS

Numerous models have been built and tested in order to achieve the goal of gaining a deeper comprehension of the kinetics involved in the release of drugs. In order to get further information regarding the rate kinetics and mechanism of drug release from the dosage form, estimated data were input into first- and zero-order Korsmeyer-Peppas release models, as well as Higuchi models. This was done.

Zero-order:

The following equation describes drug release according to zero-order kinetics.

$$F=K_o\, t$$

Where, F is the drug release at time t

K_o is rate constant of zero order

1st order release rate kinetics:

First-order drug release is being studied using the equation below.

$$\text{Log}\,(100\text{-}F) = Kt$$

Higuchi model:

Higuchi model kinetics are studied using this equation.

$$F= kt1/2$$

Pappas and Korsmeyer released model

Log percentage of released drug and time logs are shown in this model in order to examine the drug release process.

$M_t/M_\infty = Kt^n$

Where,

$N= M_t/M_\infty$ =Portion of drug released at time t

K= Constant

N= Diffusion exponent, to indicate a drug release mechanism estimated from slope of straight line. The type of drug release mechanism is characterized by n during the dissolution process.

Morphological Study

Scanning electron microscopy was used to analyse the surface characteristics of the paracetamol mucoadhesive microspheres that have been selected.

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IV. RESULT AND DISCUSSION

The purpose of this research was to find the best combination of albumin and Span 60 by 23 factorial design for Paracetamol tablet formulation, with the end goal of achieving NLT 85% dissolving in 10 minutes. The 23-factorial design uses CD, Albumin, and Span 60 to determine the optimal dose of telmisartan in a tablet.

Table 2: Physical Properties of Paracetamol tablets Prepared with Albumin & Span 60

Batch code	Hardness	Friability	Disintegration	Drug Content
FS1	4.6	0.31	345	98.2
FS2	4.1	0.32	356	100.2
FS3	5.2	0.84	345	98.4
FS4	4.9	0.70	20	99.4
FS5	4.6	0.90	156	98.1
FS6	4.4	0.85	104	99.2

Paracetamol pills had a hardness between 4.1 and 5.2 kg/cm2. No sample had a Friability index of more than 0.93 percent. All manufactured pills contain paracetamol concentrations within 3% of 100. Paracetamol pill disintegration and solubility was found to vary widely.

Table 3: Pre-formulation parameters of Core blend

FormulationCode.	Angle ofRepose	Bulk density (gm/ml)	Tapped density(gm/ml)	Carr's index (%)	Hausner'sRatio
F1	24.42	0.50±0.03	0.52±0.06	15.31±0.08	0.76±0.05
F2	24.52	0.47±0.07	0.55±0.07	15.86±0.06	0.97±0.06
F3	24.65	0.52±0.03	0.57±0.06	18.12±0.02	0.54±0.08
F4	24.45	0.48±0.08	0.55±0.08	16.77±0.09	1.22±0.05
F5	24.43	0.57±0.09	0.57±0.03	15.82±0.05	1.3±0.09
F6	25.32	0.55±0.05	0.55±0.08	18.68±0.08	1.07±0.10

The impact of a number of preformulation variables on the final mixtures were investigated. The angle of repose revealed that the tablet powder had good flow properties. In bulk, the density ranges from 0.430.07 to 0.580.06 grammes per cubic centimetre. The density of the tapped area ranges from 0.57% to 0.69%. The findings revealed that the values of the Carrs' index ranged from 16 to 18. The range of the Hausner ratio is 0 to 1.2. These elements aid in ensuring that the powder used to create tablets has acceptable flow characteristics.

Drug Release Studies of In-Vitro

Table 4: Telmisartan tablets produced with CMEC at various concentrations are dispersed

TIME. (hr.)	Cumulative Percent % Of Dissolved Drug (n=3±SD)		
	F1.	**F2.**	**F3.**
0.7	26.6	21.2	15.6
1.	45.8	38.5	25.8
2	75.6	56.4	35.8
3	98.78	76.4	45.6
4		88.5	56.6
5		98.6	66.5
6			86.5
7			92.6
8			98.24

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Zero-order; Korsmeyer-Peppas release; and Higuchi-model.

Table 5: Release kinetics data for optimized formulation

CUMULATIVE (%) RELEASE. Q	TIME. (T.)	LOG. (%) RELEASE	LOG. (%) REMAIN	RELEASE RATE. (CUMULATIVE % RELEASE / t)	1/CUM.% RELEASE	PEPPAS. log Q/100	% Drug. Remaining
00	00		3.0000				100.00
13.52	00.5	1.267	1.852	28.250	00.0588	-0.757	86.37
18.78	1	1.386	1.844	18.780	0.0608	-0.805	81.12
23.36	2	1.258	1.795	12.285	0.0548	-0.742	78.68
33.48	3	1.587	1.578	11.463	0.5348	-0.405	60.45
40.9	4	1.510	1.678	9.852	0.4755	-0.500	61.5
46.29	5	1.567	1.859	9.153	0.7227	-0.354	55.78
57.36	6	1.876	1.726	9.805	0.0477	-0.335	43.78
65.84	7	1.725	1.462	9.438	0.0342	-0.277	35.37
73.25	8	1.766	1.847	8.826	0.0246	-0.156	29.65
78.55	9	1.769	1.287	8.482	0.0342	-0.225	25.50
85.28	10	1.827	1.352	8.438	0.0432	-0.187	16.73
86.2	11	1.855	1.214	7.849	0.0216	-0.470	14.10
98.2	12	1.875	0.692	8.109	0.0354	-0.038	4.8

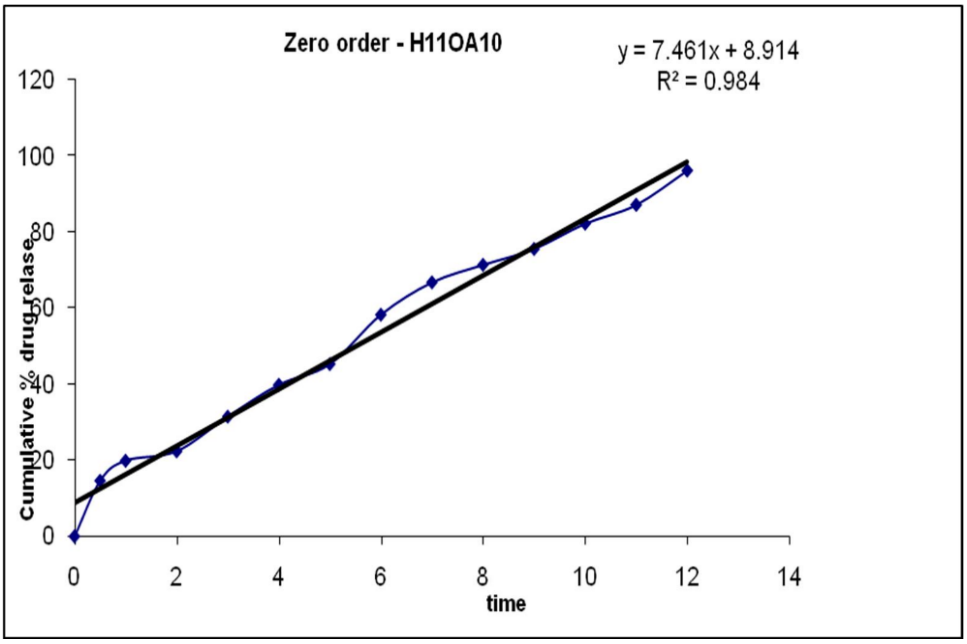

Figure 4: Kinetics Graph of Zero order release

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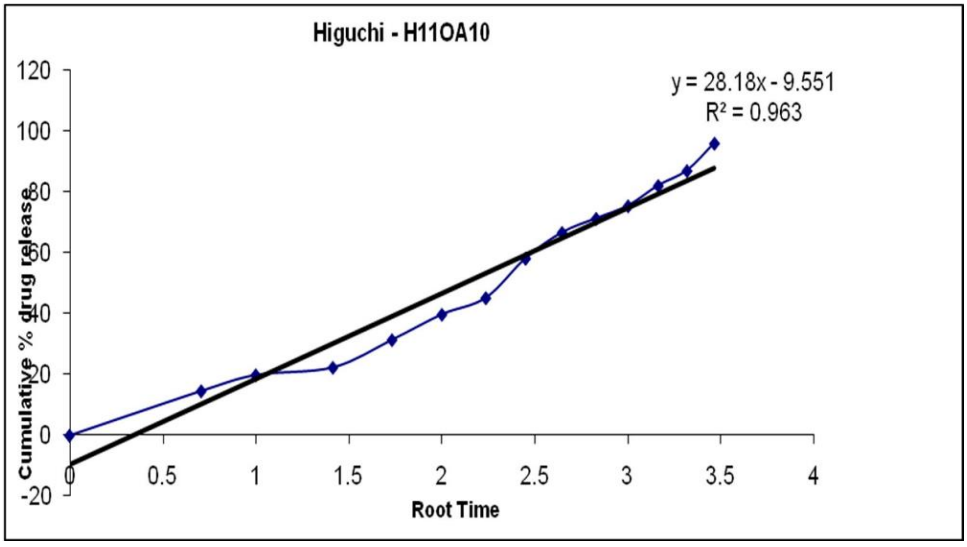

Figure 5: Kinetics graph of Higuchi release

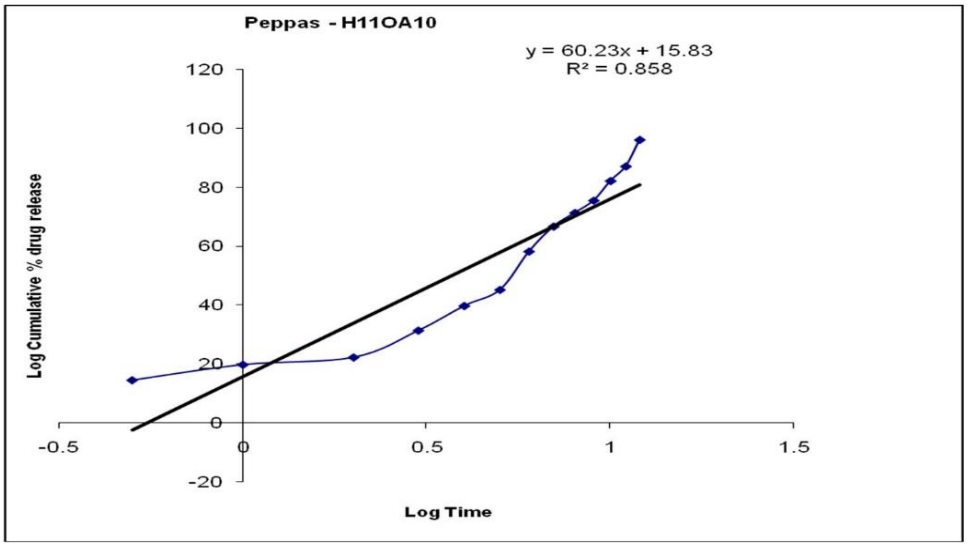

Figure 6: Graph of Korsmeyer-Peppas

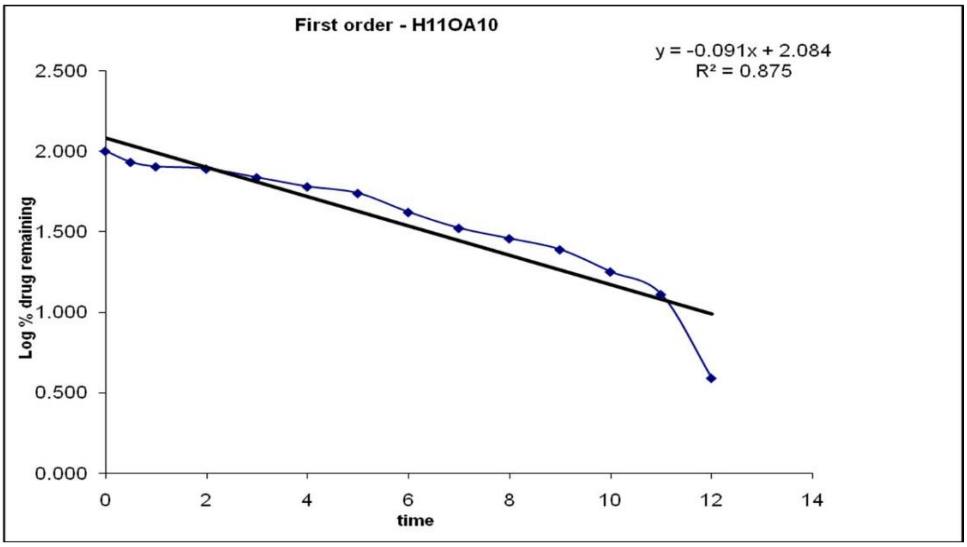

Figure 7: Kinetics graph of First order release

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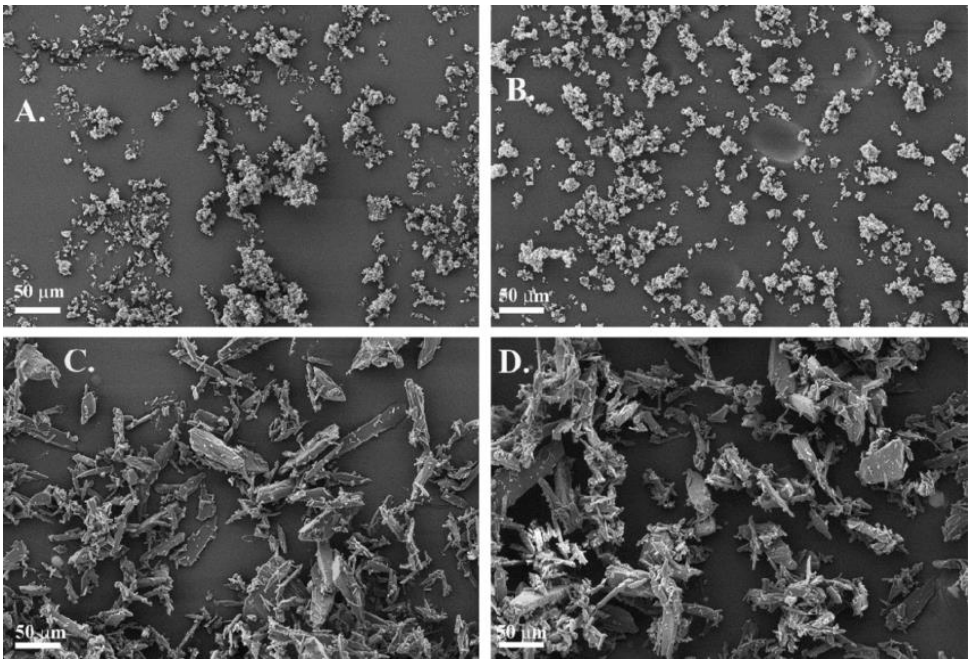

Figure 8: SEM image of paracetamol tablets granules

V. CONCLUSION

According to the investigation's findings, the prepared paracetamol oral disintegrating tablets dissolve more uniformly and in vitro more quickly than the industry standard product. As a result, it can be assumed that the study's tablets, which quickly dissolve and cover up their bitter taste, may make it easier to administer paracetamol without water during emesis. It should be used to develop more therapeutic choices because the existing drug delivery strategy may improve patient compliance in comparison to conventional tablets.

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